REMARKS

Favorable reconsideration is respectfully requested in view of the foregoing amendments and the following remarks.

I. CLAIM STATUS AND AMENDMENTS

Claims 44-55, 58, 59, 61, 63-65, and 68 are pending.

Claims 44-54 were withdrawn as non-elected subject matter.

Claims 55, 58, 59, 61, 63-65, and 68 were examined on the merits and stand rejected. Claim 59 was objected to.

Claim 59 is amended in a non-narrowing manner to spell out the full name of "Tomato yellow leaf curl Sardinia virus" before the abbreviation "TYLCSV" as supported by the disclosure at page 2, line 9.

Claim 65 is amended in a non-narrowing manner to rephrase the claim to remove the parenthesis around "SEQ ID No 9" as suggested by the Examiner.

Claim 68 is amended in a non-narrowing manner to use proper Markush style format.

No new matter has been added by the above claim amendments.

The originally filed specification and abstract have been replaced with attached substitute specification. The substitute specification corrects grammatical and spelling errors throughout and adds appropriate section headings to conform to

U.S. practice. The abstract has been revised to reflect the elected claimed invention as supported by the disclosure at page 14, lines 22-36. No new matter has been added.

Applicants note that the above amendments are intended to address matters of form only as they are not intended to affect the scope of the claims. Accordingly, if the next Office Action on the merits includes a new ground of rejection of one or more claims, the Action must be non-final.

II. OBJECTIONS TO THE ABSTRACT AND SPECIFICATION

The specification and abstract were objected for not including a reference 26 for the reason in item 1 on page 2 of the Office Action.

The present amendment overcomes these objections by replacing the originally filed specification and abstract with attached substitute specification and abstract. The substitute specification corrects inadvertent grammatical and spelling errors and adds appropriate section headings to conform to U.S. practice. The Abstract is revised to conform to US practice. Support can be found in the disclosure, at page 14, lines 25-36.

III. CLAIM OBJECTIONS

Claims 59 and 65 were objected to for the minor informalities noted in items 5-6 on page 4 of the Office Action.

Claim 59 is amended to spell out the full name of "Tomato yellow leaf curl Sardinia virus" before the abbreviation "TYLCSV" as suggested by the Examiner. Support can be found in the disclosure at page 2, line 9.

Claim 65 is amended in a non-narrowing manner to rephrase the claim to remove the parenthesis around "SEQ ID No 9" as suggested by the Examiner.

Thus, it is believed that the present amendment overcomes the noted objections. Withdrawal of the objections is requested.

IV. INDEFINITENESS REJECTION

Claims 55, 58-59, 61, 63-65, and 68 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for the reasons in item 7 on page 5 of the Office Action. This rejection is traversed.

Applicants respectfully submit that the skilled artisan would clearly understand the term "long lasting resistance" in claim 55 in view of the guidance in the disclosure and the knowledge of the art. It is well established that definiteness of claim language is analyzed, not in a vacuum, but in light of the teachings of the prior art and of the particular application disclosure as it would be interpreted by one possessing the ordinary level of skill in the pertinent art. In re Moore, 439

F.2d 1232, 169 USPQ 236 (CCPA 1971). See also, M.P.E.P., Eighth Ed., Rev. 6 (September 2007) at § 2173.02.

Throughout the disclosure, the ability of the claimed invention to achieve long lasting resistance to geminivirus is discussed. For instance, the specification at page 29, Table 8, describes such long lasting resistance when agro-inoculated with an TYLCSV infectious clone as shown from the comparison of the resistant plants at 3 and 12 weeks after inoculation. The specification at other locations also discusses resistance weeks after inoculation. Further, it should be noted that the Office, in item 8 at page 5 of the Action, acknowledges that the specification is enabling for "preparation of transgenic plant having long lasting resistance." Thus, it would seem that even the Office comprehends the metes and bounds of the term "long lasting". Thus, it is respectfully submitted that the skilled artisan would clearly understand what is meant by the phrase "long lasting resistance."

The Office has objected to claim 55 on the basis that the end of the claim does not correlate to the preamble. Applicants respectfully disagree. Step (c) of claim 55 requires "insertion of the geminivirus gene sequence mutated in the step b) in the plant, plant tissue or cell thereof, using a construct comprising an heterologous polynucleotide sequence containing in the 5'-3' direction." It is well understood by those skilled in

the art that this step produces a transgenic plant. As such, it is not believed necessary to further amend the claims.

The claims are thus clear, definite and have full antecedent basis. The rejection is believed to be overcome, and withdrawal thereof is respectfully requested.

V. ENABLEMENT REJECTION

Claims 55, 58, 59, 61, 63-65, and 68 were rejected under 35 U.S.C. § 112, first paragraph, on the basis that the specification is enabling for a method for the preparation of transgenic plant having long lasting resistance against gemininviruses by making silent mutations to truncated Rep gene from TYLCSV, but not for making any mutations to truncated Rep gene from TYLCSV having 130 residues from N-terminal or the Rep protein, or any geminivirus-derived sequence encoding an amino acid sequence able to confer resistance against geminiviruses. See item 8 on pages 6-10 of the Office Action.

This rejection is respectfully traversed.

As acknowledged by the Office, the specification enables a method for preparing a transgenic plant having long lasting resistance against geminiviruses by making silent mutations to truncated Rep gen from TYLCSV. Applicants appreciate the Examiner's indication, but respectfully submit that the specification also enables the full scope of the claims for at least the reasons noted below.

The specification describes in detail that a unifying feature of the invention is the introduction of silent point mutations derived by geminiviruses and distributed in such a way that the length of the regions with continuous homology between the new mutated sequence and the original one is below or equal to 8 nucleotides, or below or equal to 5 nucleotides. This is clearly reflected in step (b) of independent claim 55. This method allows one skilled in the art to obtain a new nucleotide sequence having the same codifying capability of the original sequence, but having a different nucleotide sequence in such a way that it is an ineffective target of the gene silencing induced by the virus, thereby producing a long lasting resistance.

It should be noted that the present application is not directed to, nor does it not claim, a generic site-specific mutagenesis on geminivirus sequences. On the contrary, the present application claims only a specific typology of mutations, that consist of silent point mutations distributed in such a way that the length of the regions with continuous homology between the new mutated sequence and the original one is below or equal to 8 nucleotides, and preferably below or equal to 5 nucleotides. Thus, contrary to the Office's assertion the claims are not directed to just "any" mutation to truncated Rep gene from TYLCSV having 130 residues from the N-terminal of the Rep protein or any

geminivirus-derived sequence encoding an amino acid able to confer resistance against geminiviruses.

Further, it is believed that the claimed method for obtaining transgenic plants having long lasting resistance against geminivirus should not be restricted only to TYLCSV and SEQ ID Nos 8 and 9. In this regard, the method according to the invention can be used to all Begomovirus that can infect tomato. Indeed, as it is well known, that proteins derived from geminivirus AL1/C1/AC1 gene are able to interfere with the replication of the respective virus. However, the resistances obtained by the expression of protein derived by the AL1/C1/AC1 gene are not lasting because the viral transgene is silenced by the infecting virus. This has also been shown in TYLCV (Antignus et al., 2004, Annals of Applied Biology) or in ACMV (Sangarè et al., 1999, Molecular Biology Reports).

Also, the method according to the present invention is independent from the sequence. In fact, it is applicable to all AL1/C1/AC1 geminivirus gene sequences and all the more reason it is applicable to the Begomovirus subclass that infects tomato, as demonstrated with TYLCSV in the example according to the invention.

For instance, the specification at the top of page 9 describes in detail that the gene sequences from which constructing the polynucleotide sequence according to the invention can be obtained from the geminiviruses such as,

Mastrevirus, Curtovirus, Begomovirus, Topocuvirus and particularly can be derived from the species shown in table 4 and their isolates, more particularly from the species of Tomato yellow leaf curl and their isolates shown in table 5. Some preferable species are also listed at the bottom of page 12 and the top of page 13.

The specification at pages 13-14 also describes in detail that the gene sequence belonging to the genome of the geminiviruses can be the sequence C1/AL1/AC1, C2/AL2/AC2, C3/AL3/AC3, C4/AL4/AC4, V1/AR1/AV1, V2/AR2/AV2, BC1/BL1 and BV1/BR1, particularly, the sequence C1/AL1/AC1 of the previously described geminiviruses and their isolates. At this location, the specification also discloses that the amino acid sequence encoded by the polynucleotide sequence object of the present invention is a pathogen-derived protein able to confer resistance against the geminiviruses to the plants expressing it. Said interfering protein since, according to the invention, is stably expressed, confers a lasting resistance independently from the molecular mechanism by which the protein product is able to induce resistance. The pathogen-derived protein can be a capsid protein, replication-associated viral protein (Rep), proteins encoded by the genes C2/AL2/AC2, C3/AL3/AC3, C4/AL4/AC4, V2/AR2/AV2, BC1/BL1 and BV1/BR1.

The specification also discloses that an example of a possible polynucleotide sequence satisfying the above reported

requirement is set forth in figures 16A and 16B that show the alignment between the wild-type nucleotide sequence encoding the Rep-210 protein of the TYLCSV and the synthetic nucleotide sequence modified so as not to be a target of the post-trascriptional degradation induced by the infecting virus, where both nucleotide sequences encode the same viral protein.

Further, on pages 14-17, the specification describes in detail the nature of the mutagenesis step and the nature of the mutations. Specific examples of mutations and truncated Rep-130 protein are given. See also the description of the various examples as depicted in Figures 1-22 and the description thereof on pages 17-20. See also Examples 1-13.

Based on the above, it is believed that the skilled artisan could extrapolate from the detailed disclosure and the examples therein to practice the full scope of the claims without undue experimentation. Thus, it is respectfully submitted that it would not constitute undue experimentation for the skilled artisan to practice the full scope of the claims given the guidance in the disclosure and the knowledge in the art.

For these reasons, it is believed that the above-noted enablement rejection should be withdrawn.

VI. OBVIOUSNESS REJECTION

Claims 55, 58, 59, 61, 63-65, and 68 were rejected under 35 U.S.C. § 102(e) as anticipated by or, in the

alternative, under 35 U.S.C. § 103(a) as obvious over POLSTON et al. (US 2005/0125862) for the reasons in item 9 on pages 11-13 of the Office Action. This rejection is respectfully traversed.

This rejection is respectfully traversed as applied to the amended claims.

The rejection should fall, because POLSTON fails to disclose or suggest each and every element of independent claim 55. In this regard, the following two aspects of the claimed invention distinguish over teachings in POLSTON: (1) protein expression from the geminiviral transgene; and (2) post-transcriptional gene silencing.

First, Applicants will discuss protein expression from the geminiviral transgene.

The present application describes in detail how to obtain transgenic plants resistant to geminivirus through the use of geminivirus-derived sequences. It is disclosed that that the geminivirus sequences selected for their ability to induce resistance to geminiviruses need to be expressed at the protein level. Also, previous literature published by the Applicants (Noris et al. 1996 "Resistance to tomato yellow leaf curl geminivirus in Nicotiana benthamiana plants transformed with a truncated viral C1 gene," Virology, 224(1):130-8; Erratum in: Virology 1997,227(2):519; Brunetti et al., 1997, "High expression of truncated viral Rep protein confers resistance to tomato yellow leaf curl virus in transgenic tomato plants," Mol Plant

Microbe Interact 10, 571-579) showed that transgenic lines carrying geminiviral sequences that are not expressed at detectable levels or that are in antisense orientation with respect to the promoter are not virus resistant.

Accordingly, a high level of protein expression from the geminiviral transgene is therefore important for inducing resistance. This concept is discussed in the instant application at page 4, line 32 as: "It's clear that the best strategy in order to obtain plants resistant to a wide spectrum of geminiviruses is the one in which the interfering product is the protein." See also Examples 5 to 8, where plants showing resistance are expressing the transgene at the protein level).

POLSTON fails to disclose or suggest this novel aspect of the claimed invention.

Instead, in POLSTON, the resistant phenotype is related to the kind of sequences introduced into plants and to the presence of the transgenes in plants (see Tables 1-4in POLSTON). However, there is no mention in POLSTON to the level of transgene expression.

Further, POLSTON even discloses sequences that are in antisense orientation with respect to the promoter. This arrangement rules out the involvement of protein expression in the induction of resistance (see POLSTON at claims 1, 22, 44 and depending claims.

For these reasons, it is believed that the above features distinguish the claimed method over POLSTON.

Applicants will now discuss post-transcriptional gene silencing. By way of the present application, Applicants have further demonstrated that upon geminivirus infection in experimental or natural conditions, geminiviral gene sequences undergo post-transcriptional gene silencing, as a defense reaction exerted by plants towards virus infection (see Example 1 of our specification). This implies that any geminivirus sequence introduced as a transgene into a plant or a plant cell and sharing a high level of identity to the viral genome can undergo post-transcriptional gene silencing, upon even a minimal geminiviral infection. A consequence of this phenomenon is that the efficacy of the expressed transgene can be reduced or completely disallowed.

It is believed that this novel aspect of the invention is no where mentioned in POLSTON.

Yet, from this, Applicants designed a method devoted to avoid the virus-induced post-transcriptional gene silencing with the aim of maintaining a sustained level of expression of the geminivirus-derived sequences in transgenic plants. This is reflected in step (b) of claim 55, which involves introducing point silent mutations (see Example 9 of our specification) "so that the continuous homology between the mutated sequence and corresponding viral gene sequence is less than or equal to 8

nucleotides or less than or equal to 5 nucleotides" (Claim 55, point b). This is done to avoid the virus-induced post-transcriptional gene silencing and to prolong the stability of the expressed transgene sequences and, consequently, the stability/durability of the resistance-phenotype induced by the transgenes. This is clearly reflected in point (iii) of Claim 55, which recites "properly mutagenized according to step (b) to be an ineffective target of the post-transcriptional gene silencing induced by the infecting geminivirus". It is respectfully submitted that this novel feature of claimed method is no where mentioned or suggested in POLSTON.

For these reasons, it is clear that it was not the Applicants' intent to introduce silent mutation in the geminivirus Rep-derived sequence to "provide codon preference in a specific host cell" (as stated in paragraph [0038] of POLSTON, for optimizing host cell expression. Based on such, it is believed that, contrary to the Office's position, POLSTON fails to teach the above-noted novel features of the claimed method.

In fact, at Paragraph [0038], POLSON discloses introducing silent mutations in their polynucleotide sequence only to "provide codon preference in a specific host cell". POLSTON does not mention the role of point mutations in avoiding post-transcriptional gene silencing. Accordingly, POLSTON does not disclose the above-noted novel features of the claims.

For these reasons, it is believed that the independent claim 55 and all claims dependent thereon are novel and patentable over POLSTON. Thus, withdrawal of the rejection is requested.

VII. CONCLUSION

Having addressed all the outstanding issues, the amendment is believed to be fully responsive. In view of the above, it is respectfully submitted that the application is in condition for allowance and notice to that effect is hereby requested. If the Examiner has any comments or proposals for expediting prosecution, please contact the undersigned attorney at the telephone number below.

The Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 25-0120 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17.

Respectfully submitted,

YOUNG & THOMPSON

/Jay F. Williams/

Jay F. Williams, Reg. No. 48,036
209 Madison Street, Suite 500
Alexandria, VA 22314
Telephone (703) 521-2297
Telefax (703) 685-0573
(703) 979-4709

JFW

APPENDIX:

The Appendix includes the following item(s):

X - a Substitute Specification and a marked-up copy of the originally-filed specification